Electronic Supplementary Information for Flexible Synthesis, Structural Determination, and Synthetic Application of a New C_1-Symmetric Chiral Ammonium Betaine

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General Information: Infrared spectra were recorded on a JASCO FT/IR-300E spectrometer. ^1H NMR spectra were recorded on a Varian Mercury-300BB (300 MHz), a Varian INOVA-500 (500 MHz) or Varian INOVA-700 (700 MHz) spectrometer. Chemical shifts are reported in ppm from the solvent resonance [$(CD_3)_2SO$; 2.50 ppm, CD_3OD; 3.31 ppm, C_6D_6; 7.16 ppm] or Me_4Si resonance (0.0 ppm; $CDCl_3$, $(CD_3)_2CO$) as the internal standard. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, br = broad) and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian INOVA-500 (126 MHz) or a Varian INOVA-700 (175 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance [$(CD_3)_2CO$; 29.84 ppm, $(CD_3)_2SO$; 39.51 ppm, CD_3OD; 49.00 ppm, $CDCl_3$; 77.16 ppm, C_6D_6; 128.06 ppm]. Optical rotations were measured on a JASCO DIP-1000 polarimeter. The high resolution mass spectra were conducted on JEOL JMS-700 (MStation). Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm). Flash column chromatography was performed on silica gel 60 (spherical, 40-50 μm; Kanto Chemical Co., Inc.). Enantiomeric excesses were determined by HPLC analysis using chiral columns [ϕ 4.6 mm x 250 mm, DAICEL CHIRALPAK AD-H (AD-H) or CHIRALPAK IA (IA)].

Toluene, THF, Et_2O, and CH_2Cl_2 were supplied from Kanto Chemical Co., Inc. as “Dehydrated solvent system”. Aromatic and heteroaromatic imines,[1] and 2-alkoxythiazol-5(4*H*)-ones[2] were prepared by following the literature procedure. Other simple chemicals were purchased and used as such.

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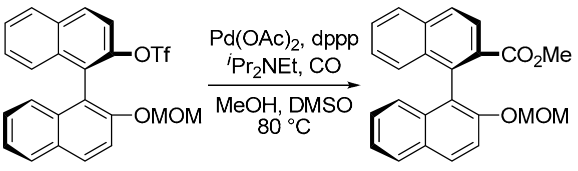
[1] A. G. Wenzel, E. N. Jacobsen, *J. Am. Chem. Soc.*, 2002, **124**, 12964.
[2] Y. Lin, K. K. Andersen, *Eur. J. Org. Chem.*, 2002, 557.

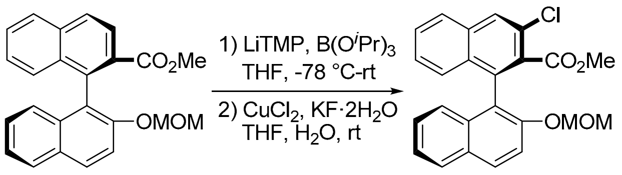
Experimental Section:

(1) Preparation and Characterization of C_1-Symmetric Chiral Ammonium Betaine 1:



2 **3**

Representative procedure for preparation of 3[3]**:** A solution of **2**[4] (6.5 g, 14.0 mmol), Pd(OAc)$_2$ (472.5 mg, 2.1 mmol), and dppp (948.6 mg, 2.31 mmol) in DMSO (70.0 mL) was evacuated and backfilled with argon. Then, ^{i}Pr$_2$NEt (10.6 mL, 62.0 mmol) and MeOH (28.0 mL) were added and the mixture was stirred for 24 h at 80 °C. After being cooled to room temperature, the resulting mixture was poured into H_2O and extracted with ethyl acetate (EA) twice. The combined organic extracts were washed with H_2O twice and brine, and dried over Na_2SO_4. Evaporation of volatiles and subsequent purification of the residue by column chromatography on silica gel [hexane (H)/EA = 20:1-5:1 as eluent] afforded **3** (3.7 g, 9.94 mmol, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (1H, d, J = 8.5 Hz), 7.98 (1H, d, J = 8.5 Hz), 7.94 (1H, d, J = 8.5 Hz), 7.92 (1H, d, J = 8.5 Hz), 7.85 (1H, d, J = 8.5 Hz), 7.55 (1H, d, J = 8.5 Hz), 7.51 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.32 (1H, d, J = 8.5 Hz), 7.31 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.26 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.17 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 6.97 (1H, d, J = 8.5 Hz), 5.05 (1H, d, J = 6.5 Hz), 4.96 (1H, d, J = 6.5 Hz), 3.46 (3H, s), 3.08 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.8, 151.8, 137.3, 135.2, 134.0, 133.1, 129.6, 129.5, 128.9, 128.0_5, 128.0_2, 127.8_4, 127.7_9, 126.7, 126.5, 126.2, 125.2, 124.0, 123.5, 116.5, 94.9, 55.9, 51.9, one carbon was not found probably due to overlapping; IR (neat): 3060, 2950, 1727, 1333, 1278, 1241, 1150, 1035, 1014, 908, 768, 732 cm^{-1}; HRMS (FAB) Calcd for $C_{24}H_{20}O_4$ ($[M+H]^+$) 372.1362. Found 372.1364.



3 **4**

Representative procedure for preparation of 4: B(O^{i}Pr)$_3$ (5.7 mL, 25.0 mmol) and a solution of **3** (3.7 g, 10.0 mmol) in THF (10.0 mL) were sequentially introduced to a THF solution of lithium 2,2,6,6-tetramethylpiperidine (LiTMP) (ca. 1 M, 20 mL, 20.0 mmol) at −78 °C. The resulting reaction mixture was allowed to warm to room temperature without removing cooling bath and poured into saturated NH_4Cl aqueous solution. The aqueous phase was extracted with EA twice and the combined organic extracts were washed with brine. After drying over Na_2SO_4 and filtration, the organic phase was concentrated under vacuum. The residual solid was mixed with $CuCl_2$ (2.7 g, 20.0 mmol) and $KF\cdot 2H_2O$ (941.3 mg, 10.0 mmol), and the whole materials were dissolved into 80%

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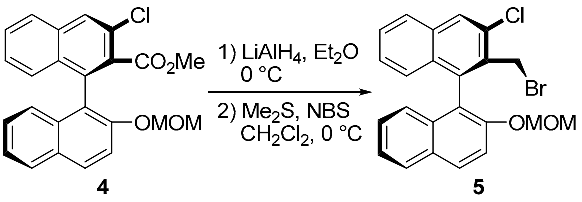
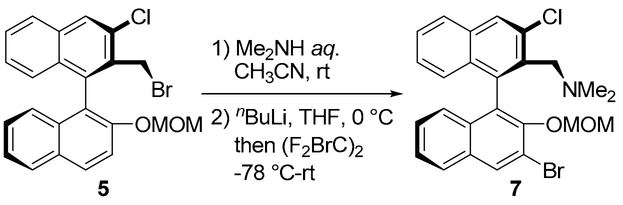
[3] T. Ohta, M. Ito, K. Inagaki, H. Takaya, *Tetrahedron Lett.*, 1993, **34**, 1615.
[4] T. Ooi, K. Ohmatsu, K. Maruoka, *J. Am. Chem. Soc.*, 2007, **129**, 2410.

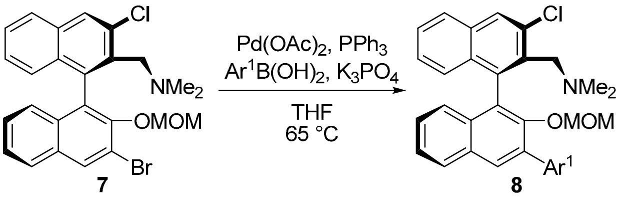
aqueous THF (30.0 mL). After degassing process, the mixture was stirred overnight. The resulting mixture was quenched by the addition of saturated NH_4Cl aqueous solution and extracted with EA twice. The combined organic phasees were washed with brine and dried over Na_2SO_4. Filtration and concentration were performed, and the crude product was purified by column chromatography on silica gel (H/EA = 20:1-5:1 as eluent) to give **4** (2.1 g, 5.1 mmol, 51%) as a white solid. **4:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (1H, s), 7.94 (1H, d, J = 8.5 Hz), 7.84 (1H, d, J = 8.5 Hz), 7.83 (1H, d, J = 8.5 Hz), 7.56 (1H, d, J = 8.5 Hz), 7.51 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.33 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.28 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.25 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.24 (1H, d, J = 8.5 Hz), 7.07 (1H, d, J = 8.5 Hz), 5.11 (1H, d, J = 7.0 Hz), 5.02 (1H, d, J = 7.0 Hz), 3.31 (3H, s), 3.22 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 153.0, 135.3, 134.1, 133.7, 132.7, 131.3, 130.6, 129.3, 128.0, 127.8_1, 127.7_9, 127.6, 127.4, 127.1, 127.0, 126.8, 125.6, 124.2, 120.2, 116.0, 94.9, 56.0, 52.0; IR (neat): 3060, 2951, 1737, 1280, 1243, 1137, 1072, 1034, 1014, 909, 733 cm^{-1}; HRMS (FAB) Calcd for $C_{24}H_{19}O_4Cl$ ($[M+H]^+$) 406.0972. Found 406.0980.



Representative procedure for preparation of 5: To a suspension of $LiAlH_4$ (174.6 mg, 4.6 mmol) in Et_2O (23.0 mL) was added **4** (934.0 mg, 2.3 mmol) portionwise at 0 °C and the reaction mixture was stirred for 1 h at 0 °C. The reaction was quenched by the sequential treatment with H_2O (174.6 μL), 15% NaOH aqueous solution (174.6 μL), and H_2O (523.8 μL). After being stirred for 1 h at room temperature, this mixture was filtered through a pad of Celite and the filtrate was concentrated. Without further purification, this crude was used for the subsequent bromination. To a suspension of NBS (2.0 g, 11.5 mmol) in CH_2Cl_2 (11.5 mL) was added Me_2S (845.0 μL, 11.5 mmol) dropwise at 0 °C and the yellow mixture was stirred for 10 min at 0 °C. The crude alcohol was added portionwise at 0 °C. The reaction mixture was stirred for 24 h at 0 °C and poured into saturated $NaHCO_3$ aqueous solution. Extractive workup was performed with $CHCl_3$ and the combined extracts were dried over Na_2SO_4. Removal of volatiles and purification of the residue by column chromatography on silica gel (H/EA = 50:1-5:1 as eluent) furnished **5** (840.4 mg, 1.9 mmol, 83% in two steps) as a white solid. **5:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (1H, s), 8.01 (1H, d, J = 8.5 Hz), 7.89 (1H, d, J = 8.5 Hz), 7.81 (1H, d, J = 8.5 Hz), 7.64 (1H, d, J = 8.5 Hz), 7.47 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.36 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.24 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.22 (1H, ddd, J = 8.5, 7.0, 1.5 Hz), 7.11 (1H, d, J = 8.5 Hz), 6.96 (1H, d, J = 8.5 Hz), 5.15 (1H, d, J = 7.0 Hz), 5.00 (1H, d, J = 7.0 Hz), 4.51 (1H, d, J = 10.0 Hz), 4.39 (1H, d, J = 10.0 Hz), 3.17 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 137.3, 133.9, 133.5, 132.5, 132.2, 131.9, 130.7, 129.7, 128.5, 128.1, 127.6, 127.2, 127.0, 126.8, 125.4, 124.5, 120.5, 116.2, 95.0, 56.1, 30.0, one carbon was not found probably due to overlapping; IR (neat): 2954, 1593, 1508, 1243, 1149, 1071, 1034, 1014, 992, 907, 749 cm^{-1}; HRMS (FAB) Calcd for $C_{23}H_{18}O_2ClBr$ ($[M+H]^+$) 440.0179. Found 440.0179.



Representative procedure for preparation of 7: Bromide **5** (220.0 mg, 0.5 mmol) was treated with 50% aqueous Me_2NH (262.0 µL, 2.5 mmol) in MeCN (5.0 mL) for 1 h at room temperature. The reaction mixture was diluted with H_2O and extracted with $CHCl_3$ twice. The organic extracts were washed with brine, dried over Na_2SO_4, and concentrated. Residual crude product of **6** was satisfactory pure in NMR for the next reaction. To a solution of the crude **6** in THF (5.0 mL) was added a solution of ^{n}BuLi in hexane (1.6 M, 780.0 µL, 1.25 mmol) dropwise at 0 °C and the solution was stirred for 30 min. After being cooled to −78 °C, the reaction mixture was treated with 1,2-dibromo-1,1,2,2-tetrafluoroethane (188.0 µL, 1.5 mmol). The resulting reaction mixture was warmed to room temperature, diluted with saturated NH_4Cl aqueous solution, and extracted with EA twice. The organic extracts were dried, filtered, and concentrated. The residual solid was purified by column chromatography on silica gel (H/EA = 20:1-2:1 as eluent) to give **7** (201.7 mg, 0.4 mmol, 83% in two steps) as a yellow highly viscous liquid. **7:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (1H, s), 8.06 (1H, s), 7.81$_2$ (1H, d, J = 8.5 Hz), 7.80$_6$ (1H, d, J = 8.5 Hz), 7.46 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.41 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.24 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.22 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.11 (1H, d, J = 8.5 Hz), 7.06 (1H, d, J = 8.5 Hz), 4.77 (1H, d, J = 5.5 Hz), 4.56 (1H, d, J = 5.5 Hz), 3.73 (1H, d, J = 13.0 Hz), 3.12 (1H, d, J = 13.0 Hz), 2.58 (3H, s), 1.83 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 135.3, 135.2, 134.2, 133.2, 133.1$_3$, 133.0$_8$, 132.1, 131.5, 129.7, 128.8, 127.2, 127.1, 126.8, 126.7, 126.5, 126.1, 117.4, 98.9, 59.2, 56.6, 45.7, two carbons were not found probably due to overlapping; IR (neat): 2939, 2817, 2766, 1160, 1002, 970, 930, 749 cm^{-1}; HRMS (FAB) Calcd for $C_{25}H_{24}NO_2BrCl^+$ ($[M+H]^+$) 486.0659. Found 486.0667.



Representative procedure for preparation of 8: To a test tube were placed **7** (48.5 mg, 0.1 mmol), p-Tip-$C_6H_4B(OH)_2$[5] (**B1**, 48.6 mg, 0.15 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), PPh_3 (2.6 mg, 0.01 mmol), and K_3PO_4 (84.9 mg, 0.4 mmol). After the addition of THF (0.35 mL), evacuation and refill with argon were repeated three times and the reaction mixture was stirred for 18 h at 65 °C. The reaction mixture was filtered through a pad of Celite at room temperature. The concentrated filtrate was purified by column chromatography on silica gel (H/EA = 20:1-2:1 as eluent) to afford **8d** (50.6 mg, 0.74 mmol, 74%) as a white solid.

8a (Ar^1 = Ph)**:** 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (1H, s), 7.97 (1H, s), 7.89 (1H, d, J = 8.5 Hz), 7.79

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[5] Tip = 2,4,6-triisopropylphenyl. For preparation of the boronic acid, see below.

(1H, d, J = 8.5 Hz), 7.71 (2H, d, J = 7.5 Hz), 7.46 (2H, t, J = 7.5 Hz), 7.43 (1H, dt, J = 8.5, 4.0 Hz), 7.41-7.35 (2H, m), 7.24-7.19 (3H, m), 7.09 (1H, d, J = 8.5 Hz), 4.23 (1H, d, J = 6.0 Hz), 4.19 (1H, d, J = 6.0 Hz), 3.76 (1H, d, J = 13.0 Hz), 3.37 (1H, d, J = 13.0 Hz), 2.17 (3H, s), 1.94 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.6, 139.0, 136.4, 135.2, 134.3, 133.4, 133.2, 132.1, 131.0, 130.8, 129.7, 129.6, 128.6, 128.4, 128.0$_8$, 128.0$_6$, 127.6, 127.5, 127.0, 126.7, 126.6, 126.4, 126.2, 125.3, 98.4, 59.5, 55.9, 45.8; IR (neat): 2939, 2766, 1158, 996, 976, 933, 751 cm^{-1}; HRMS (FAB) Calcd for $C_{31}H_{29}NO_2Cl^+$ ($[M+H]^+$) 482.1887. Found 482.1902.

8d (Ar^1 = p-^{t}Bu-C_6H_4)**:** 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (1H, s), 7.97 (1H, s), 7.89 (1H, d, J = 8.0 Hz), 7.79 (1H, d, J = 8.0 Hz), 7.64 (2H, d, J = 8.5 Hz), 7.49 (2H, d, J = 8.5 Hz), 7.44 (1H, dt, J = 8.0, 4.0 Hz), 7.39 (1H, t, J = 8.0 Hz), 7.23-7.19 (3H, m), 7.07 (1H, d, J = 8.0 Hz), 4.25 (1H, d, J = 6.0 Hz), 4.20 (1H, d, J = 6.0 Hz), 3.73 (1H, d, J = 13.5 Hz), 3.36 (1H, d, J = 13.5 Hz), 2.16 (3H, s), 1.94 (6H, s), 1.37 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.8, 150.6, 136.5, 136.0, 135.2, 135.0, 134.3, 133.3, 133.2, 132.2, 131.0, 130.8, 129.1, 128.4, 128.1, 128.0, 127.7, 127.0, 126.7, 126.6, 126.3, 126.2, 125.5, 125.3, 98.4, 59.5, 55.8, 45.8, 34.7, 31.5; IR (neat): 2962, 2764, 1457, 1391, 1158, 1078, 998, 976, 837, 750 cm^{-1}; HRMS (FAB) Calcd for $C_{35}H_{37}NO_2Cl^+$ ($[M+H]^+$) 538.2513. Found 538.2488.

8e (Ar^1 = p-Mes-C_6H_4)[6]**:** 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (1H, s), 8.05 (1H, s), 7.92 (1H, d, J = 8.0 Hz), 7.80 (1H, d, J = 8.0 Hz), 7.77 (2H, d, J = 8.0 Hz), 7.44 (1H, ddd, J = 8.0, 5.5, 3.0 Hz), 7.41 (1H, t, J = 8.0 Hz), 7.28-7.19 (5H, m), 7.10 (1H, d, J = 8.0 Hz), 6.97 (2H, s), 4.27 (1H, d, J = 6.0 Hz), 4.24 (1H, d, J = 6.0 Hz), 3.79 (1H, d, J = 13.0 Hz), 3.38 (1H, d, J = 13.0 Hz), 2.34 (3H, s), 2.26 (3H, s), 2.05 (6H, s), 1.94 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.8, 140.3, 138.8, 137.2, 136.8, 136.3, 136.0, 135.3, 135.0, 134.3, 133.4, 133.2, 132.1, 131.0, 130.9, 129.7, 129.5, 128.5, 128.3, 128.1, 128.0, 127.6, 127.0, 126.7$_2$, 126.6$_7$, 126.4, 126.3, 125.3, 98.4, 59.5, 56.0, 45.8, 21.2, 20.9; IR (neat): 2938, 2765, 1454, 1389, 1158, 998, 975, 842, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{40}H_{39}NO_2Cl^+$ ($[M+H]^+$) 600.2669. Found 600.2686.

8f (Ar^1 = p-Tip-C_6H_4)**:** 74% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (1H, s), 8.06 (1H, s), 7.93 (1H, d, J = 8.0 Hz), 7.81 (1H, d, J = 8.0 Hz), 7.76 (2H, d, J = 8.0 Hz), 7.45 (1H, ddd, J = 8.0, 5.5, 2.5 Hz), 7.41 (1H, t, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz), 7.25-7.20 (2H, m), 7.22 (1H, ddd, J = 8.0, 6.5, 1.5 Hz), 7.09$_4$ (1H, d, J = 8.0 Hz), 7.08$_6$ (2H, s), 4.26 (1H, d, J = 5.5 Hz), 4.24 (1H, d, J = 5.5 Hz), 3.81 (1H, d, J = 13.0 Hz), 3.38 (1H, d, J = 13.0 Hz), 2.96 (1H, sept, J = 7.0 Hz), 2.69 (2H, sept, J = 7.0 Hz), 2.32 (3H, s), 1.93 (6H, s), 1.32 (6H, d, J = 7.0 Hz), 1.10$_3$ (6H, d, J = 7.0 Hz), 1.09$_9$ (6H, d, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.9, 148.1, 146.6, 140.1, 137.2, 136.9, 136.3, 135.4, 135.0, 134.4, 133.4, 133.3, 132.1, 131.0, 130.9, 130.0, 129.3, 128.5, 128.1, 128.0, 127.6, 127.1, 126.7$_4$, 126.6$_8$, 126.3$_4$, 126.3$_2$, 125.4, 120.7, 98.5, 59.5, 56.0, 45.8, 34.4, 30.5, 24.3$_4$, 24.2$_8$, 24.2; IR (neat): 2959, 2766, 1458, 1362, 1158, 1077, 998, 976, 844, 753 cm^{-1}; HRMS (FAB) Calcd for $C_{46}H_{51}NO_2Cl^+$ ($[M+H]^+$) 684.3608. Found 684.3624.

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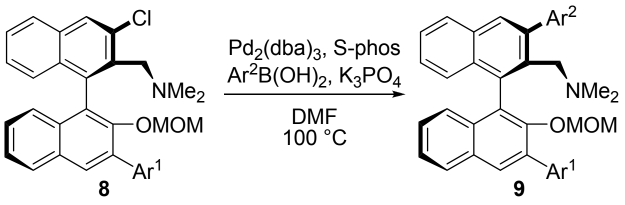
[6] Mes = 2,4,6-trimethylphenyl



Representative procedure for preparation of 9: To a test tube were placed **8f** (68.4 mg, 0.1 mmol), $PhB(OH)_2$ (24.4 mg, 0.2 mmol), Pd_2dba_3 (4.58 mg, 0.005 mmol), S-phos[7] (8.21 mg, 0.02 mmol), and K_3PO_4 (84.9 mg, 0.4 mmol). After the addition of DMF (0.2 mL), evacuation and refill with argon were repeated three times and the reaction mixture was stirred for 24 h at 100 °C. The reaction mixture was filtered through a pad of Celite at room temperature and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (H/EA = 20:1-2:1 as eluent) to give **9f** (71.4 mg, 0.098 mmol, 98%) as a white solid.

9a (Ar^1 = Ph, Ar^2 = Ph)**:** 44% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (1H, s), 7.88 (1H, d, J = 8.0 Hz), 7.85 (1H, d, J = 8.0 Hz), 7.80 (1H, s), 7.72 (2H, d, J = 7.5 Hz), 7.49 (2H, d, J = 7.5 Hz), 7.46 (2H, t, J = 7.5 Hz), 7.44-7.33 (4H, m), 7.42 (2H, t, J = 7.5 Hz), 7.26-7.17 (4H, m), 4.29 (1H, d, J = 5.5 Hz), 4.21 (1H, d, J = 5.5 Hz), 3.52 (1H, d, J = 13.0 Hz), 3.33 (1H, d, J = 13.0 Hz), 2.26 (3H, s), 1.55 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.1, 143.1, 142.2, 139.3, 136.3, 135.4, 134.4, 134.0, 132.9, 132.5, 130.8, 130.4, 129.7, 129.6, 129.5, 129.4, 128.5, 127.9, 127.8, 127.7, 127.4, 127.2, 127.1, 126.6, 126.0, 125.9, 125.8, 125.1, 98.4, 58.6, 55.9, 44.9; IR (neat): 2929, 2853, 2762, 1454, 1157, 993, 971, 934, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{37}H_{34}NO_2^+$ ($[M+H]^+$) 524.2590. Found 524.2573.

9c (Ar^1 = Ph, Ar^2 = p-^{t}Bu-C_6H_4)**:** 71% yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (1H, s), 7.88 (1H, d, J = 8.4 Hz), 7.84 (1H, d, J = 8.4 Hz), 7.82 (1H, s), 7.72 (2H, d, J = 8.4 H), 7.48-7.34 (9H, m), 7.26-7.18 (4H, m), 4.28 (1H, d, J = 5.6 Hz), 4.19 (1H, d, J = 5.6 Hz), 3.54 (1H, brd, J = 11.2 Hz), 3.36 (1H, brd, J = 11.2 Hz), 2.25 (3H, s), 1.55 (6H, s), 1.39 (9H, s); ^{13}C NMR (175 MHz, $CDCl_3$) δ 149.8, 149.3, 142.0, 139.8, 139.2, 136.3, 135.3, 134.2, 133.8, 132.6, 132.3, 130.7, 130.1, 129.5_1, 129.4_5, 129.3, 129.2, 128.3, 127.7, 127.6, 127.2, 127.0_1, 126.9_8, 125.7, 125.6_2, 125.5_9, 124.9, 124.3, 98.2, 58.4, 55.8, 44.8, 34.5, 31.4; IR (neat): 2961, 2762, 1456, 1158, 994, 973, 751 cm^{-1}; HRMS (FAB) Calcd for $C_{41}H_{42}NO_2^+$ ($[M+H]^+$) 580.3216. Found 580.3215.

9d (Ar^1 = p-^{t}Bu-C_6H_4, Ar^2 = Ph)**:** 66% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (1H, s), 7.87 (1H, d, J = 8.5 Hz), 7.84 (1H, d, J = 8.5 Hz), 7.80 (1H, s), 7.66 (2H, d, J = 8.0 Hz), 7.48_7 (2H, d, J = 8.0 Hz), 7.47_9 (2H, d, J = 8.0 Hz), 7.42 (2H, t, J = 8.0 Hz), 7.42-7.34 (3H, m), 7.26 (1H, d, J = 8.5 Hz), 7.23 (1H, t, J = 8.5 Hz), 7.20 (1H, t, J = 8.5 Hz), 7.17 (1H, d, J = 8.5 Hz), 4.32 (1H, d, J = 5.5 Hz), 4.21 (1H, d, J = 5.5 Hz), 3.51 (1H, d, J = 13.5 Hz), 3.34 (1H, d, J = 13.5 Hz), 2.25 (3H, s), 1.54 (6H, s), 1.37 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.4, 150.2, 143.1, 142.2, 136.3, 135.3, 134.5, 133.8, 132.9, 132.5, 130.9, 130.3, 129.6, 129.4_2, 129.3_9, 129.2, 127.9, 127.8, 127.7, 127.2, 127.1, 126.6, 125.9, 125.8, 125.4, 125.0, 98.4, 58.6, 55.9, 44.9, 34.7, 31.5, two carbons were not found probably due to overlapping; IR (neat): 2960, 2813, 2761, 1463, 1158, 994, 972, 837, 751 cm^{-1}; HRMS (FAB) Calcd for $C_{41}H_{42}NO_2^+$ ($[M+H]^+$) 580.3216. Found 580.3243.

9e (Ar^1 = p-Mes-C_6H_4, Ar^2 = Ph)**:** 59% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (1H, s), 7.91 (1H, d, J = 8.5

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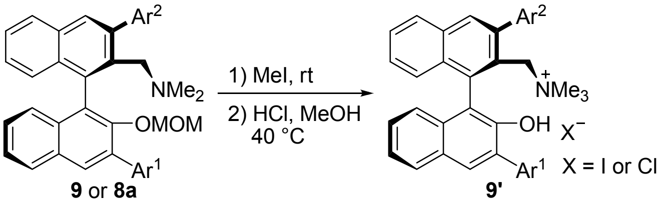
[7] 2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl

Hz), 7.86 (1H, d, J = 8.5 Hz), 7.81 (1H, s), 7.78 (2H, d, J = 8.0 Hz), 7.49 (2H, d, J = 8.0 Hz), 7.45-7.38 (4H, m), 7.36 (1H, t, J = 8.5 Hz), 7.28 (1H, d, J = 8.5 Hz), 7.26-7.20 (4H, m), 7.19 (1H, d, J = 8.5 Hz), 6.97 (2H, s), 4.33 (1H, d, J = 5.5 Hz), 4.26 (1H, d, J = 5.5 Hz), 3.54 (1H, d, J = 13.0 Hz), 3.35 (1H, d, J = 13.0 Hz), 2.35 (3H, s), 2.34 (3H, s), 2.05 (6H, s), 1.55 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.3, 143.1, 142.3, 140.2, 138.9, 137.6, 136.8, 136.3, 136.1, 135.4, 134.4, 134.0, 132.9, 132.5, 130.9, 130.3, 129.8, 129.6, 129.4, 128.3, 127.9_2, 127.8_7, 127.7, 127.2, 127.1, 126.6, 126.0, 125.9_3, 125.8_7, 125.1, 98.5, 58.6, 56.1, 45.0, 21.2, 20.9, two carbons were not found probably due to overlapping; IR (neat): 2932, 2853, 2763, 1455, 1157, 994, 972, 842, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{46}H_{44}NO_2^+$ ([M+H]$^+$) 642.3372. Found 642.3376

9f (Ar^1 = p-Tip-C_6H_4, Ar^2 = Ph)**:** 98% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (1H, s), 7.91 (1H, d, J = 8.5 Hz), 7.86 (1H, d, J = 8.5 Hz), 7.81 (1H, s), 7.76 (2H, d, J = 8.0 Hz), 7.50 (2H, d, J = 8.0 Hz), 7.43 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.42 (2H, t, J = 8.0 Hz), 7.40 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.36 (1H, t, J = 8.0 Hz), 7.30 (2H, d, J = 8.0 Hz), 7.28 (1H, d, J = 8.5 Hz), 7.24 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.22 (1H, ddd, J = 8.5, 6.5, 1.5 Hz), 7.18 (1H, d, J = 8.5 Hz), 7.08 (2H, s), 4.33 (1H, d, J = 5.5 Hz), 4.27 (1H, d, J = 5.5 Hz), 3.55 (1H, d, J = 13.0 Hz), 3.35 (1H, d, J = 13.0 Hz), 2.96 (1H, sept, J = 7.0 Hz), 2.70 (2H, sept, J = 7.0 Hz), 2.40 (3H, s), 1.54 (6H, s), 1.32 (6H, d, J = 7.0 Hz), 1.11 (6H, d, J = 7.0 Hz), 1.10 (6H, d, J = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.4, 148.1, 146.7, 143.1, 142.3, 139.9, 137.5, 137.0, 136.3, 135.5, 134.4, 134.0, 132.9, 132.5, 130.9, 130.3, 129.9, 129.6, 129.5, 129.4_5, 129.3_6, 127.9, 127.6, 127.2, 126.6, 126.0, 125.9_2, 125.8_8, 125.1, 120.7, 98.5, 58.6, 56.1, 45.0, 34.4, 30.5, 24.4, 24.3, 24.2, two carbons were not found probably due to overlapping; IR (neat): 2959, 2867, 2762, 1459, 1362, 1157, 1073, 994, 972, 935, 844, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{52}H_{56}NO_2^+$ ([M+H]$^+$) 726.4311. Found 726.4317.



Representative procedure for preparation of 9': Amine **9f** was dissolved into MeI (1.0 mL) at room temperature and the solution was stirred for 6 h. After removal of excess MeI, the residual solid was treated with 1 M HCl methanolic solution (1.0 mL) at 40 °C for 12 h. The concentrated crude solid was purified by column chromatography on silica gel (H/EA = 1:1 then $CHCl_3$/MeOH = 1:0-5:1 as eluent) to give **9'f** quantitatively.

9'a (Ar^1 = Ph, Ar^2 = Ph)**:** ^{1}H NMR (700 MHz, $(CD_3)_2SO$, 80 °C) δ 8.74 (1H, brs), 8.13 (1H, d, J = 7.7 Hz), 8.12 (1H, s), 8.09 (1H, s), 8.04 (1H, d, J = 7.7 Hz), 7.69 (2H, d, J = 7.7 Hz), 7.68-7.64 (3H, m), 7.63 (2H, t, J = 7.7 Hz), 7.54 (1H, t, J = 7.7 Hz), 7.51 (2H, t, J = 7.7 Hz), 7.45 (1H, t, J = 7.7 Hz), 7.43 (1H, t, J = 7.7 Hz), 7.41 (1H, t, J = 7.7 Hz), 7.36 (1H, t, J = 7.7 Hz), 7.28 (1H, d, J = 7.7 Hz), 6.94 (1H, d, J = 7.7 Hz), 4.89 (1H, br), 4.45 (1H, br), 2.54 (9H, brs); ^{13}C NMR (175 MHz, $(CD_3)_2SO$, 80 °C) δ 150.0, 140.9, 140.8, 138.9, 137.6, 133.7, 132.4, 131.8, 131.5, 131.0, 130.9, 129.6, 129.1, 128.7, 128.3, 127.9, 127.8, 127.6, 127.5, 127.0, 126.9, 126.5, 124.5, 123.4, 123.1, 117.7, 64.3, 53.5, two carbons were not found probably due to overlapping; IR (neat): 3055, 2930, 1620, 1486, 1427, 1327, 1238, 1216, 1189, 1127, 1029, 899, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{36}H_{32}NO^+$ ([M-X]$^+$) 494.2484. Found 494.2493.

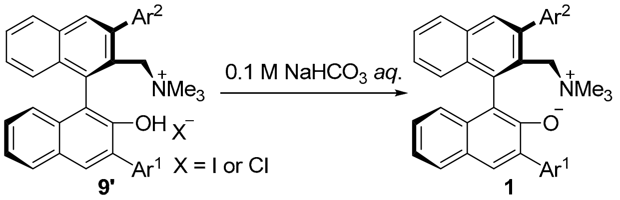
9’b (Ar^1 = Ph, Ar^2 = Cl)**:** ^{1}H NMR (700 MHz, $(CD_3)_2SO$, 80 °C) δ 8.80 (1H, brs), 8.47 (1H, s), 8.11 (1H, d, J = 7.7 Hz), 8.10 (1H, s), 8.03 (1H, d, J = 7.7 Hz), 7.69 (1H, t, J = 7.7 Hz), 7.67 (2H, d, J = 7.7 Hz), 7.50 (2H, t, J = 7.7 Hz), 7.46 (1H, t, J = 7.7 Hz), 7.42 (1H, t, J = 7.7 Hz), 7.39 (1H, t, J = 7.7 Hz), 7.31 (1H, t, J = 7.7 Hz), 7.23 (1H, d, J = 7.7 Hz), 6.75 (1H, br), 4.83 (1H, br), 4.47 (1H, br), 2.98 (9H, brs); ^{13}C NMR (175 MHz, $(CD_3)_2SO$, 80 °C) δ 150.0, 140.7, 137.5, 134.4, 132.5, 132.1, 131.7, 131.2_1, 131.1_8, 129.3_2, 129.2_9, 129.0, 128.4, 128.3, 128.2, 127.7, 127.3, 127.1, 127.0, 126.6, 124.7, 123.5, 122.7, 116.8, 64.8, 53.5; IR (neat): 3186, 3049, 2928, 1620, 1484, 1427, 1183, 1125, 882, 749 cm^{-1}; HRMS (FAB) Calcd for $C_{30}H_{27}NOCl^+$ ($[M-X]^+$) 452.1781. Found 452.1788.

9’c (Ar^1 = Ph, Ar^2 = p-^{t}Bu-C_6H_4)**:** ^{1}H NMR (700 MHz, $(CD_3)_2SO$, 80 °C) δ 8.72 (1H, br), 8.12 (1H, s), 8.11 (1H, d, J = 7.7 Hz), 8.04 (1H, d, J = 7.7 Hz), 7.70 (2H, d, J = 7.7 Hz), 7.65 (1H, t, J = 7.7 Hz), 7.64 (2H, d, J = 7.7 Hz), 7.59 (2H, d, J = 7.7 Hz), 7.51 (2H, t, J = 7.7 Hz), 7.46-7.39 (4H, m), 7.35 (1H, t, J = 7.7 Hz), 7.27 (1H, d, J = 7.7 Hz), 6.93 (1H, d, J = 7.7 Hz), 4.89 (1H, br), 4.46 (1H, br), 2.53 (9H, s), 1.46 (9H, s); ^{13}C NMR (175 MHz, $(CD_3)_2SO$, 80 °C) δ 150.4, 149.9, 140.8, 138.8, 137.9, 137.6, 133.8, 132.4, 131.8, 131.5, 130.9, 130.8, 129.3, 129.1, 129.0, 128.3, 127.9, 127.7, 127.6, 127.0, 126.8, 126.4, 125.4, 124.8, 123.4, 123.1, 117.7, 64.4, 53.6, 34.0, 30.7; IR (neat): 3381, 2961, 1621, 1487, 1192, 1128, 890, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{40}H_{40}NO^+$ ($[M-X]^+$) 550.3110. Found 550.3098.

9’d (Ar^1 = p-^{t}Bu-C_6H_4, Ar^2 = Ph)**:** ^{1}H NMR (700 MHz, $(CD_3)_2SO$, 80 °C) δ 8.71 (1H, brs), 8.13 (1H, d, J = 7.7 Hz), 8.12 (1H, s), 8.08 (1H, s), 8.02 (1H, d, J = 7.7 Hz), 7.70-7.61 (7H, m), 7.54 (1H, t, J = 7.7 Hz), 7.53 (2H, d, J = 7.7 Hz), 7.44 (1H, t, J = 7.7 Hz), 7.40 (1H, t, J = 7.7 Hz), 7.35 (1H, t, J = 7.7 Hz), 7.28 (1H, d, J = 7.7 Hz), 6.93 (1H, d, J = 7.7 Hz), 4.88 (1H, br), 4.44 (1H, br), 2.54 (9H, brs), 1.38 (9H, s); ^{13}C NMR (175 MHz, $(CD_3)_2SO$, 80 °C) δ 150.1, 149.6, 140.9, 140.8, 139.0, 134.6, 133.7, 132.2, 131.6, 131.5, 131.0, 130.8, 129.6, 128.7_3, 128.7_0, 128.3, 128.2, 127.9, 127.6, 127.5, 126.9, 126.8, 126.5, 124.6, 124.5, 123.4, 123.0, 117.7, 64.3, 53.5, 33.9, 30.7; IR (neat): 3055, 2960, 1618, 1484, 1447, 1401, 1237, 1128, 1027, 899, 753 cm^{-1}; HRMS (FAB) Calcd for $C_{40}H_{40}NO^+$ ($[M-X]^+$) 550.3104. Found 550.3105.

9’e (Ar^1 = p-Mes-C_6H_4, Ar^2 = Ph)**:** ^{1}H NMR (700 MHz, $(CD_3)_2SO$, 80 °C) δ 8.80 (1H, brs), 8.19 (1H, s), 8.14 (1H, d, J = 7.7 Hz), 8.13 (1H, s), 8.07 (1H, d, J = 7.7 Hz), 7.79 (2H, d, J = 7.7 Hz), 7.67 (2H, d, J = 7.7 Hz), 7.66 (1H, t, J = 7.7 Hz), 7.63 (2H, t, J = 7.7 Hz), 7.54 (1H, t, J = 7.7 Hz), 7.45 (1H, t, J = 7.7 Hz), 7.42 (1H, t, J = 7.7 Hz), 7.36 (1H, t, J = 7.7 Hz), 7.29 (1H, d, J = 7.7 Hz), 7.25 (2H, d, J = 7.7 Hz), 6.96_4 (2H, s), 6.95_6 (1H, d, J = 7.7 Hz), 4.90 (1H, br), 4.54 (1H, br), 2.56 (9H, brs), 2.30 (3H, s), 2.05 (6H, s); ^{13}C NMR (175 MHz, $(CD_3)_2SO$, 80 °C) δ 150.0, 140.9, 140.8, 139.4, 138.9, 137.9, 135.8, 135.5, 134.7, 133.7, 132.3, 131.5, 131.0_3, 130.9_8, 129.6, 129.0, 128.7, 128.6, 128.4, 128.3, 127.9, 127.6, 127.5_3, 127.4_7, 127.0, 126.9, 126.5, 124.5, 123.4, 123.2, 117.8, 64.3, 53.5, 20.1, 19.9, one carbon was not found probably due to overlapping; IR (neat): 3012, 2922, 1615, 1482, 1434, 1236, 1126, 1004, 847, 753 cm^{-1}; HRMS (FAB) Calcd for $C_{45}H_{42}NO^+$ ($[M-X]^+$) 612.3266. Found 612.3293.

9’f (Ar^1 = p-Tip-C_6H_4, Ar^2 = Ph)**:** ^{1}H NMR (700 MHz, $(CD_3)_2SO$, 80 °C) δ 8.85 (1H, brs), 8.22 (1H, s), 8.14 (1H, d, J = 7.7 Hz), 8.13 (1H, s), 8.08 (1H, d, J = 7.7 Hz), 7.78 (2H, d, J = 7.7 Hz), 7.67 (2H, d, J = 7.7 Hz), 7.66 (1H, t, J = 7.7 Hz), 7.63 (2H, t, J = 7.7 Hz), 7.54 (1H, t, J = 7.7 Hz), 7.45 (1H, t, J = 7.7 Hz), 7.42 (1H, t, J = 7.7 Hz), 7.36 (1H, t, J = 7.7 Hz), 7.31-7.26 (3H, m), 7.10 (2H, s), 6.95 (1H, d, J = 7.7 Hz), 4.89 (1H, br), 4.59 (1H, br), 2.95 (1H, sept, J = 7.0 Hz), 2.71 (2H, sept, J = 7.0 Hz), 2.56 (9H, brs), 1.29 (6H, d, J = 7.0 Hz), 1.10 (12H, d, J = 7.0 Hz); ^{13}C NMR (175 MHz, $(CD_3)_2SO$, 80 °C) δ 150.0, 147.2, 145.7, 140.9_2, 140.8_6, 139.2, 138.8, 136.1, 135.8, 133.7, 132.4, 131.5, 131.0, 129.6, 129.0, 128.7, 128.6, 128.4, 128.3, 127.9, 127.6, 127.5, 127.0, 126.9, 126.5, 124.6, 123.4, 123.1, 119.8, 117.8, 64.3, 53.5, 33.1, 29.3$_7$, 29.3$_6$, 23.6, 23.4, two carbons were not found probably due to overlapping; IR (neat): 2959, 2868, 1618, 1469, 1361, 1217, 1128, 1005, 877, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{51}H_{54}NO^+$ ($[M-X]^+$) 696.4205. Found 696.4221.



Representative procedure for preparation of 1: A solution of **9'f** (ca. 0.1 mmol) in EA (5.0 mL) was washed with 0.1 M $NaHCO_3$ aqueous solution (20.0 mL) three times. The resulting yellow organic phase was dried over Na_2SO_4, filtered, and concentrated to furnish crude betaine. Washing it with ether on a funnel followed by drying under vacuum afforded **1f** as a yellow powder (57.0 mg, 0.082 mmol, 82%).

1a (Ar^1 = Ph, Ar^2 = Ph)**:** 74% yield (3 steps). ^{1}H NMR (700 MHz, CD_3OD) δ 7.95 (br), 7.94 (br), 7.90 (br), 7.82 (br), 7.72 (d, J = 7.7 Hz), 7.67 (br), 7.58 (br), 7.53 (t, J = 7.7 Hz), 7.48 (br), 7.38 (br), 7.26 (d, J = 7.7 Hz), 7.11 (br), 6.98 (br), 6.63 (br), 5.10 (d, J = 14.0 Hz), 4.98 (br), 4.94 (d, J = 14.0 Hz), 4.45 (br), 2.63 (br), 2.34 (br); IR (KBr): 3025, 1605, 1582, 1487, 1424, 1391, 1227, 969, 887, 759 cm^{-1}; HRMS (FAB) Calcd for $C_{36}H_{32}NO^+$ ($[M+H]^+$) 494.2484. Found 494.2477.

1b (Ar^1 = Ph, Ar^2 = Cl)**:** 76% yield (3 steps). ^{1}H NMR (300 MHz, CD_3OD) δ 8.22 (br), 7.95 (br), 7.93 (br), 7.87 (br), 7.76 (br), 7.72 (br), 7.59 (t, J = 7.5 Hz), 7.40 (t, J = 7.5 Hz), 7.29 (t, J = 7.5 Hz), 7.09 (br), 6.62 (br), 6.51 (br), 4.98-4.76 (br), 4.41 (br), 3.08 (br), 2.83 (br); IR (KBr): 3021, 1608, 1583, 1487, 1421, 1281, 1150, 975, 880, 748 cm^{-1}; HRMS (FAB) Calcd for $C_{30}H_{27}NOCl^+$ ($[M+H]^+$) 452.1781. Found 452.1784.

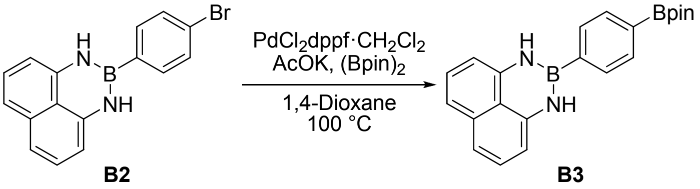
1c (Ar^1 = Ph, Ar^2 = p-^{t}Bu-C_6H_4)**:** 72% yield (3 steps). ^{1}H NMR (700 MHz, CD_3OD) δ 8.55 (br), 7.97 (d, J = 8.4 Hz), 7.96 (br), 7.92 (br), 7.87 (br), 7.81 (br), 7.76 (br), 7.70 (br), 7.68 (d, J = 8.4 Hz), 7.64 (br), 7.58 (br), 7.57 (d, J = 8.4 Hz), 7.45 (d, J = 8.4 Hz), 7.44-7.36 (m), 7.36-7.32 (m), 7.30 (br), 7.22 (br), 7.16 (br), 7.04 (br), 6.77 (br), 6.68 (br), 5.16 (d, J = 14.7 Hz), 5.10 (d, J = 14.7 Hz), 4.38 (d, J = 14.7 Hz), 2.63 (brs), 2.35 (brs), 1.40 (s); IR (KBr): 2961, 1609, 1486, 1416, 1386, 1224, 889, 750 cm^{-1}; HRMS (FAB) Calcd for $C_{40}H_{40}NO^+$ ($[M+H]^+$) 550.3110. Found 550.3105.

1d (Ar^1 = p-^{t}Bu-C_6H_4, Ar^2 = Ph)**:** 78% yield (3 steps). ^{1}H NMR (500 MHz, CD_3OD) δ 7.97 (br), 7.96 (br), 7.94 (br), 7.90 (br), 7.82 (br), 7.75 (br), 7.71 (d, J = 7.5 Hz), 7.67 (br), 7.58 (br), 7.54 (t, J = 7.5 Hz), 7.49 (br), 7.43 (d, J = 7.5 Hz), 7.38 (br), 7.28 (br), 7.10 (br), 6.98 (br), 6.63 (br), 5.10 (d, J = 13.0 Hz), 5.04-4.91 (br), 4.45 (br), 2.62 (br), 2.34 (br), 1.36 (s); IR (KBr): 3025, 2959, 1607, 1583, 1486, 1425, 1203, 1151, 891, 831, 756 cm^{-1}; HRMS (FAB) Calcd for $C_{40}H_{40}NO^+$ ($[M+H]^+$) 550.3110. Found 550.3113.

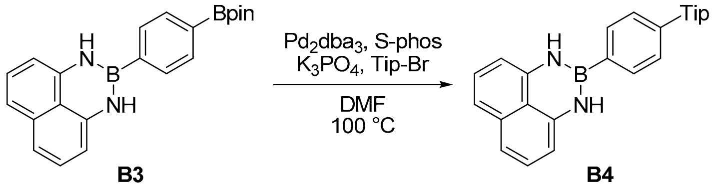
1e (Ar^1 = p-Mes-C_6H_4, Ar^2 = Ph)**:** 81% yield (3 steps). ^{1}H NMR (500 MHz, CD_3OD) δ 7.99 (br), 7.97 (br), 7.96 (br), 7.92 (br), 7.85 (br), 7.77 (br), 7.69 (br), 7.59 (br), 7.50 (br), 7.39 (br), 7.29 (br), 7.14 (d, J = 7.5 Hz), 7.06 (br), 7.01 (br), 6.92 (s), 6.66 (br), 5.13 (d, J = 14.0 Hz), 5.03 (br), 4.95 (d, J = 14.0 Hz), 4.47 (br), 2.66 (br), 2.37 (br), 2.30 (s), 2.04 (s); IR (KBr): 3023, 1606, 1581, 1483, 1425, 1389, 1279, 1150, 1003, 835, 745 cm^{-1}; HRMS (FAB) Calcd for $C_{45}H_{42}NO^+$ ($[M+H]^+$) 612.3266. Found 612.3237.

1f (Ar^1 = *p*-Tip-C_6H_4, Ar^2 = Ph)**:** 82% yield (3 steps). ^{1}H NMR (500 MHz, CD_3OD) δ 7.98 (br), 7.96 (br), 7.93 (br), 7.82 (br), 7.79 (br), 7.68 (br), 7.59 (br), 7.57 (br), 7.51 (br), 7.41 (br), 7.31 (br), 7.18 (d, *J* = 8.0 Hz), 7.06 (s), 7.02 (br), 6.73 (br), 6.67 (br), 5.13 (d, *J* = 14.5 Hz), 5.04 (br), 4.93 (d, *J* = 14.5 Hz), 4.45 (br), 2.92 (sept, *J* = 7.0 Hz), 2.78 (br), 2.67 (br), 2.37 (br), 1.29 (d, *J* = 7.0 Hz), 1.09 (d, *J* = 7.0 Hz); IR (KBr): 3020, 2958, 1605, 1581, 1468, 1426, 1389, 1203, 838, 747 cm^{-1}; HRMS (FAB) Calcd for $C_{51}H_{54}NO^+$ ($[M+H]^+$) 696.4205. Found 696.4221.

(2) Preparation of Boronic Acid B1:



Conversion of B2 to B3: Title compound was prepared from known intermediate **B2**[8] according to the literature procedure.[9] **B3:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (2H, d, *J* = 7.5 Hz), 7.63 (2H, d, *J* = 7.5 Hz), 7.12 (2H, t, *J* = 7.5 Hz), 7.04 (2H, d, *J* = 7.5 Hz), 6.39 (2H, d, *J* = 7.5 Hz), 6.03 (2H, s), 1.36 (12H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.1, 136.5, 134.5, 130.8, 127.7, 120.0, 118.0, 106.2, 84.1, 25.0, the boron-bound carbons were not detected due to quadrupolar relaxation; IR (KBr): 3424, 3372, 2979, 1600, 1528, 1392, 1360, 1321, 1235, 1141, 1094, 768 cm^{-1}.



Conversion of B3 to B4: Title compound was prepared according to the procedure for the synthesis of **9**. **B4:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (2H, d, *J* = 7.5 Hz), 7.27 (2H, d, *J* = 7.5 Hz), 7.14 (2H, t, *J* = 7.5 Hz), 7.08 (2H, s), 7.06 (2H, d, *J* = 7.5 Hz), 6.41 (2H, d, *J* = 7.5 Hz), 6.08 (2H, s), 2.95 (1H, sept, *J* = 7.0 Hz), 2.60 (2H, sept, *J* = 7.0 Hz), 1.32 (6H, d, *J* = 7.0 Hz), 1.10 (12H, d, *J* = 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.2, 146.5, 143.3, 141.3, 136.9, 136.5, 131.3, 129.9, 127.8, 120.7, 120.0, 117.9, 106.1, 34.4, 30.5, 24.4, 24.2, the boron-bound carbon was not detected due to quadrupolar relaxation; IR (KBr): 3419, 2959, 2867, 2586, 1588, 1525, 1466, 1399, 1361, 1319, 1260, 1089, 1005, 818 cm^{-1}; HRMS (FAB) Calcd for $C_{31}H_{35}N_2B^+$ ($[M+H]^+$) 446.2899, Found 446.2896.

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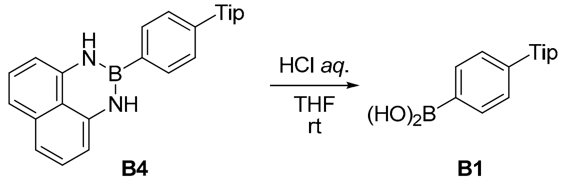
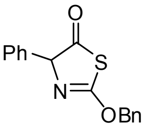
[8] H. Noguchi, K. Hojo, M. Suginome *J. Am. Chem. Soc.*, 2007, **129**, 758.

[9] N. A. Powell, F. L. Ciske, C. Cai, D. D. Holsworth, K. Mennen, C. A. Van Huis, M. Jalaie, J. Day, M. Mastronardi, P. McConnell, I. Mochalkin, E. Zhang, M. J. Ryan, J. Bryant, W. Collard, S. Ferreira, C. Gu, R. Collins, J. J. Edmunds *Bioorg. Med. Chem.*, 2007, **15**, 5912.

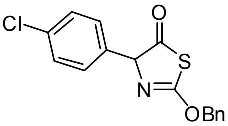


Conversion of B4 to B1: Title compound was prepared according to the literature procedure.[7] **B1:** ^{1}H NMR (500 MHz, (CD$_3$)$_2$CO) δ 7.94 (2H, d, J = 8.0 Hz), 7.18 (2H, br), 7.17 (2H, d, J = 8.0 Hz), 7.11 (2H, s), 2.95 (1H, sept, J = 7.0 Hz), 2.60 (2H, sept, J = 7.0 Hz), 1.29 (6H, d, J = 7.0 Hz), 1.06 (12H, d, J = 7.0 Hz); ^{13}C NMR (126 MHz, (CD$_3$)$_2$CO) δ 148.7, 147.0, 143.9, 138.1, 134.8, 129.8, 121.2, 35.1, 31.0, 24.5, 24.4, the boron-bound carbon was not detected due to quadrupolar relaxation; IR (KBr): 3387, 2961, 2869, 1705, 1609, 1461, 1359, 1259, 1102, 1005 cm^{-1}.

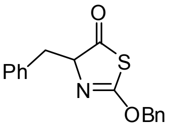
(3) Characterization of 2-Alkoxythiazol-5(4*H*)-one 10: A series of 2-Alkoxythiazol-5(4*H*)-one **10** was prepared by following the literature method.[2]



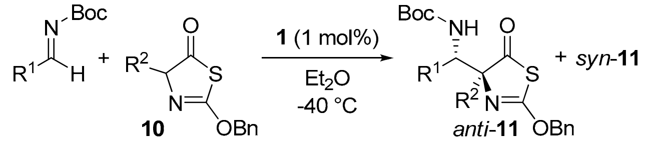
10a: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.48-7.45 (2H, m), 7.43-7.38 (3H, m), 7.38-7.32 (3H, m), 7.27-7.24 (2H, m), 5.60 (1H, s), 5.57 (1H, d, J = 12.0 Hz), 5.52 (1H, d, J = 12.0 Hz); ^{13}C NMR (126 MHz, CDCl$_3$) δ 204.5, 162.2, 135.1, 134.8, 128.9$_2$, 128.8$_7$, 128.8$_4$, 128.7$_7$, 128.7, 126.8, 83.6, 71.5; IR (neat): 1752, 1631, 1454, 1368, 1247, 1196, 1092, 1068, 908, 753 cm^{-1}; HRMS (FAB) Calcd for $C_{16}H_{14}NO_2S^+$ ([M+H]$^+$) 284.0745. Found 284.0749.



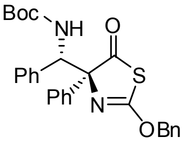
10b: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (2H, d, J = 7.5 Hz), 7.44-7.37 (3H, m), 7.31 (2H, d, J = 8.5 Hz), 7.17 (2H, d, J = 8.5 Hz), 5.57 (1H, d, J = 12.0 Hz), 5.56 (1H, s), 5.51 (1H, d, J = 12.0 Hz); ^{13}C NMR (126 MHz, CDCl$_3$) δ 204.1, 162.4, 135.0, 134.7, 133.2, 129.0, 128.9$_3$, 128.8$_6$, 128.7, 128.1, 82.8, 71.6; IR (neat): 1733, 1633, 1488, 1455, 1246, 1193, 1085, 1013, 903, 741 cm^{-1}; HRMS (FAB) Calcd for $C_{16}H_{13}NO_2SCl^+$ ([M+H]$^+$) 318.0356. Found 318.0355.

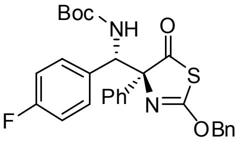


10c: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42-7.33 (5H, m), 7.26-7.19 (3H, m), 7.15-7.12 (2H, m), 5.42 (1H, d, J = 12.0 Hz), 5.33 (1H, d, J = 12.0 Hz), 4.77 (1H, dd, J = 7.0, 4.5 Hz), 3.25 (1H, dd, J = 13.5, 4.5 Hz), 3.05 (1H, dd, J = 13.5, 7.0 Hz); ^{13}C NMR (126 MHz, CDCl$_3$) δ 207.0, 160.8, 135.9, 135.2, 129.9, 128.7, 128.6, 128.3, 127.0, 81.6, 71.1, 38.7, one carbon was not found probably due to overlapping; IR (neat): 1728, 1635, 1496, 1454, 1245, 1209, 1108, 1030, 905, 740 cm^{-1}; HRMS (FAB) Calcd for $C_{17}H_{16}NO_2S^+$ ([M+H]$^+$) 298.0902. Found 298.0902.

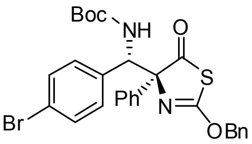


(4) Representative procedure for catalytic asymmetric Mannich-type reaction of 2-alkoxythiazol-5(4*H*)-one: To a solution of **1f** (1.39 mg, 0.002 mmol) and **10a** (56.7 mg, 0.20 mmol) in Et$_2$O (2 mL) was added benzaldehyde *N*-Boc imine (45.2 mg, 0.22 mmol) at −40 °C under argon atmosphere. After 15 min of stirring, a 0.5 M solution of trifluoroacetic acid in toluene (20.0 μL) was introduced to the reaction mixture. The resulting solution was poured into ice-cooled 1 M HCl aqueous solution and the aqueous phase was extracted with EA twice. The combined organic phases were washed with brine and dried over Na_2SO_4. After concentration to give the crude residue, the diastereomeric ratio of the product was determined by ^{1}H NMR analysis (500 MHz). Silica gel column chromatography using H/EA solvent system (H/EA = 10:1-5:1 as eluent) afforded **11a** (94.9 mg) as a mixture of diastereomers in 97% yield (*anti*/*syn* = 10:1) and the enantiomeric excess was measured by HPLC analysis. **11a:** HPLC: AD-H, H/EtOH = 32:1, flow rate = 1.0 mL/min, λ = 210 nm, 5.3 min (minor *anti* isomer), 5.7 min (major *anti* isomer), 6.4 min (major *syn* isomer), 24.4 min (minor *syn* isomer), Absolute and relative configurations were assigned by derivatization to **13** (see below); ^{1}H NMR (500 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 7.69-7.64 (2H, m), 7.58 (2H, d, J = 7.5 Hz), 7.49 (2H, t, J = 7.5 Hz), 7.45 (1H, t, J = 7.5 Hz), 7.40-7.31 (5H, m), 7.31-7.26 (3H, m), 6.42 (1H, d, J = 10.0 Hz), 5.82 (1H, d, J = 12.0 Hz), 5.78 (1H, d, J = 12.0 Hz), 5.72 (1H, d, J = 10.0 Hz), 1.18 (9H, s); ^{13}C NMR (126 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 206.4, 161.9, 155.6, 138.4, 137.1, 136.6, 129.8, 129.7, 129.5, 129.3, 129.1, 128.7, 128.6, 127.5, 94.2, 79.3, 72.5, 61.4, 28.4, one carbon was not found probably due to overlapping; IR (neat): 3438, 3017, 2979, 1712, 1635, 1494, 1367, 1217, 1169, 1076, 755 cm^{-1}; HRMS (FAB) Calcd for $C_{28}H_{29}N_2O_4S^+$ ([M+H]$^+$) 489.1848. Found 489.1866.

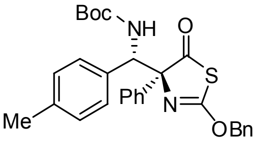




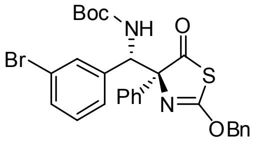
11b: HPLC: AD-H, H/2-propanol (IPA) = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 9.4 min (major *anti* isomer), 9.6 min (minor *anti* isomer), 15.0 min (minor *syn* isomer), 29.1 min (major *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 7.68-7.64 (2H, m), 7.60 (2H, d, J = 7.0 Hz), 7.51 (2H, t, J = 7.0 Hz), 7.46 (1H, t, J = 7.0 Hz), 7.42-7.30 (5H, m), 7.05 (2H, t, J = 8.5 Hz), 6.45 (1H, d, J = 9.5 Hz), 5.83 (1H, d, J = 12.0 Hz), 5.78 (1H, d, J = 12.0 Hz), 5.71 (1H, d, J = 9.5 Hz), 1.18 (9H, s); ^{13}C NMR (126 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 206.4, 163.0 (d, $J_{\text{F-C}}$ = 262.5 Hz), 162.1, 155.5, 136.9, 136.6, 134.6 (d, $J_{\text{F-C}}$ = 3.8 Hz), 131.8 (d, $J_{\text{F-C}}$ = 8.4 Hz), 129.7, 129.5$_8$, 129.5$_6$, 129.3, 129.1, 127.4, 115.4 (d, $J_{\text{F-C}}$ = 21.4 Hz), 94.1, 79.4, 72.6, 60.7, 28.3; IR (neat): 3439, 2978, 1714, 1635, 1510, 1393, 1367, 1226, 1161, 752 cm^{-1}; HRMS (FAB) Calcd for $C_{28}H_{28}N_2O_4SF^+$ ([M+H]$^+$) 507.1754. Found 507.1766.



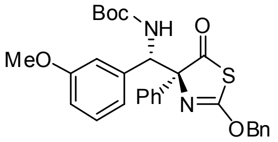
11c: HPLC: IA, H/IPA = 32:1, flow rate = 0.5 mL/min, λ = 254 nm, 7.7 min (minor *anti* isomer), 8.0 min (major *anti* isomer), 10.6 min (minor *syn* isomer), 23.0 min (major *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, C_6D_6) for major *anti* isomer δ 7.77 (2H, d, J = 7.5 Hz), 7.19 (2H, t, J = 7.5 Hz), 7.15-7.06 (8H, m), 6.76 (2H, d, J = 8.5 Hz), 5.97 (1H, d, J = 9.5 Hz), 5.46 (1H, d, J = 9.5 Hz), 5.08 (1H, d, J = 12.0 Hz), 4.91 (1H, d, J = 12.0 Hz), 1.22 (9H, s); ^{13}C NMR (126 MHz, C_6D_6) for major *anti* isomer δ 204.5, 162.8, 154.8, 136.8, 136.4, 135.5, 131.4, 130.8, 129.0$_0$, 128.9$_7$, 128.9$_1$, 128.8$_7$, 126.8, 122.3, 93.1, 79.6, 71.5, 60.5, 28.2, one carbon was not found probably due to overlapping; IR (neat): 3436, 3016, 2979, 1712, 1634, 1488, 1368, 1217, 1166, 1074, 756 cm^{-1}; HRMS (FAB) Calcd for $C_{28}H_{28}N_2O_4SBr^+$ ([M+H]$^+$) 569.0936. Found 569.0935.



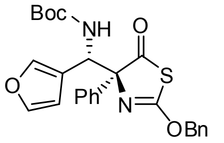
11d: HPLC: AD-H, H/IPA/EtOH = 93:2:5, flow rate = 0.5 mL/min, λ = 210 nm, 10.5 min (minor *anti* isomer), 11.1 min (major *anti* isomer), 14.5 min (minor *syn* isomer), 15.9 min (major *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 7.67-7.64 (2H, m), 7.58 (2H, d, J = 7.5 Hz), 7.49 (2H, t, *J* = 7.5 Hz), 7.45 (1H, d, *J* = 7.5 Hz), 7.40-7.34 (3H, m), 7.22 (2H, d, *J* = 8.0 Hz), 7.10 (2H, d, *J* = 8.0 Hz), 6.37 (1H, d, *J* = 10.0 Hz), 5.82 (1H, d, *J* = 12.0 Hz), 5.78 (1H, d, *J* = 12.0 Hz), 5.67 (1H, d, *J* = 10.0 Hz), 2.29 (3H, s), 1.18 (9H, s); ^{13}C NMR (126 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 206.4, 161.8, 155.5, 138.1, 137.2, 136.6, 135.5, 129.7, 129.6, 129.5, 129.3, 129.2, 129.0, 128.9, 127.4, 94.3, 79.2, 72.4, 61.2, 28.4, 21.2; IR (neat): 3438, 3011, 2978, 1714, 1635, 1494, 1367, 1226, 1168, 1072, 756 cm^{-1}; HRMS (FAB) Calcd for $C_{29}H_{31}N_2O_4S^+$ ([M+H]$^+$) 503.2005. Found 503.1993.



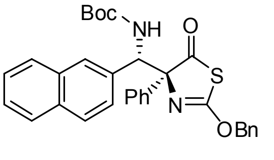
11e: HPLC: IA, H/IPA/EtOH = 98.5:0.5:1, flow rate = 0.5 mL/min, λ = 210 nm, 14.5 min (minor *anti* isomer), 16.2 min (major *anti* isomer), 18.5 min (major *syn* isomer), 23.6 min (minor *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, C_6D_6) for major *anti* isomer δ 7.77 (2H, d, *J* = 8.0 Hz), 7.57 (1H, s), 7.23-7.14 (6H, m), 7.14-7.08 (3H, m), 7.01 (1H, d, *J* = 7.5 Hz), 6.60 (1H, t, *J* = 7.5 Hz), 6.06 (1H, d, *J* = 9.5 Hz), 5.54 (1H, d, *J* = 9.5 Hz), 5.11 (1H, d, *J* = 11.5 Hz), 5.04 (1H, d, *J* = 11.5 Hz), 1.21 (9H, s); ^{13}C NMR (126 MHz, C_6D_6) for major *anti* isomer δ 204.6, 162.9, 154.8, 140.2, 136.3, 135.2, 131.9, 131.3, 129.9, 129.1, 129.0, 128.9$_3$, 128.8$_7$, 126.9, 122.3, 93.1, 79.7, 71.9, 60.7, 28.2, two carbons were not found probably due to overlapping; IR (neat): 3434, 3014, 2978, 1714, 1634, 1493, 1367, 1225, 1166, 1074, 755 cm^{-1}; HRMS (FAB) Calcd for $C_{28}H_{28}N_2O_4SBr^+$ ([M+H]$^+$) 569.0936. Found 569.0911.



11f: HPLC: AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 10.5 min (minor *anti* isomer), 11.4 min (major *anti* isomer), 15.5 min (minor *syn* isomer), 20.5 min (major *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 7.67-7.65 (2H, m), 7.56 (2H, d, *J* = 7.5 Hz), 7.48 (2H, t, *J* = 7.5 Hz), 7.43 (1H, t, *J* = 7.5 Hz), 7.40-7.32 (3H, m), 7.22 (1H, t, *J* = 7.5 Hz), 7.09 (1H, s), 6.93 (1H, d, *J* = 7.5 Hz), 6.86 (1H, d, *J* = 7.5 Hz), 6.52 (1H, d, *J* = 10.0 Hz), 5.82 (1H, d, *J* = 12.0 Hz), 5.79 (1H, d, *J* = 12.0 Hz), 5.72 (1H, d, *J* = 10.0 Hz), 3.80 (3H, s), 1.18 (9H, s); ^{13}C NMR (126 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 206.4, 161.8, 160.2, 155.6, 140.0, 137.1, 136.4, 129.7, 129.6, 129.5, 129.2, 129.0, 128.9, 127.5, 122.1, 115.6, 114.1, 94.2, 79.2, 72.5, 61.5, 55.6, 28.4; IR (neat): 3440, 3014, 2978, 1713, 1636, 1493, 1257, 1219, 1174, 1072, 756 cm^{-1}; HRMS (FAB) Calcd for $C_{29}H_{31}N_2O_5S^+$ ([M+H]$^+$) 519.1954. Found 519.1974.

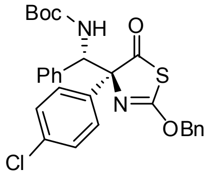


11g: HPLC: AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 10.6 min (major *anti* isomer), 11.7 min (minor *anti* isomer), 20.7 min (minor *syn* isomer), 33.7 min (major *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, C_6D_6) for major *anti* isomer δ 7.78 (2H, d, *J* = 7.5 Hz), 7.18 (2H, t, *J* = 7.5 Hz), 7.16-7.05 (6H, m), 7.02 (1H, s), 6.91 (1H, s), 6.09 (1H, d, *J* = 10.0 Hz), 5.99 (1H, s), 5.32 (1H, d, *J* = 10.0 Hz), 5.09 (1H, d, *J* = 12.0 Hz), 4.99 (1H, d, *J* = 12.0 Hz), 1.22 (9H, s); ^{13}C NMR (126 MHz, C_6D_6) for major *anti* isomer δ 204.8, 162.7, 154.8, 143.0, 141.3, 136.3, 135.5, 128.9, 128.7, 128.6, 126.9, 122.8, 110.2, 93.5, 79.4, 71.4, 53.8, 28.2, two carbons were not found probably due to overlapping; IR (neat): 3430, 2978, 1723, 1636, 1495, 1367, 1256, 1223, 1166, 1072, 754 cm^{-1}; HRMS (FAB) Calcd for $C_{26}H_{27}N_2O_5S^+$ ([M+H]$^+$) 479.1641. Found 479.1632.

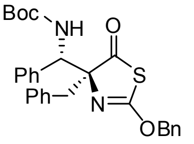


11h: HPLC: AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 11.1 min (minor *anti* isomer), 11.8 min (major *anti* isomer), 16.5 min (minor *syn* isomer), 54.4 min (major *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H

NMR (500 MHz, CD_3OD) for major *anti* isomer δ 7.79-7.71 (3H, m), 7.70-7.64 (3H, m), 7.50-7.24 (11H, m), 5.81 (1H, s), 5.69 (1H, d, J = 11.5 Hz), 5.66 (1H, d, J = 11.5 Hz), 1.19 (9H, s), N-H proton was not found probably due to deuteration; ^{13}C NMR (126 MHz, CD_3OD) for major *anti* isomer δ 207.0, 162.6, 157.1, 137.5, 136.8, 135.8, 134.3, 134.1, 129.8, 129.7, 129.6, 129.4, 129.1, 128.6, 128.5, 127.7, 127.4, 127.3, 127.2, 94.5, 80.6, 72.8, 62.3, 28.5, two carbons were not found probably due to overlapping; IR (neat): 3426, 2977, 1712, 1634, 1494, 1392, 1367, 1255, 1176, 1072, 751 cm^{-1}; HRMS (FAB) Calcd for $C_{32}H_{31}N_2O_4S^+$ ($[M+H]^+$) 539.2005. Found 539.1997.

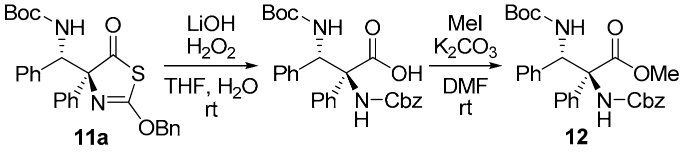


11i: HPLC: AD-H, H/EtOH = 32:1, flow rate = 1.0 mL/min, λ = 210 nm, 6.8 min (minor *anti* isomer), 7.3 min (major *anti* isomer), 9.4 min (major *syn* isomer), 16.4 min (minor *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 7.68 (2H, d, J = 9.0 Hz), 7.58 (2H, d, J = 7.0 Hz), 7.50 (2H, t, J = 7.0 Hz), 7.45 (1H, t, J = 7.0 Hz), 7.39 (2H, d, J = 9.0 Hz), 7.36 (2H, d, J = 7.0 Hz), 7.32-7.28 (3H, m), 6.55 (1H, d, J = 10.5 Hz), 5.82 (1H, d, J = 12.0 Hz), 5.78 (1H, d, J = 12.0 Hz), 5.67 (1H, d, J = 10.5 Hz), 1.19 (9H, s); ^{13}C NMR (126 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 206.3, 162.0, 155.6, 138.0, 136.5, 136.1, 134.9, 129.8, 129.6_3, 129.5_6, 129.5, 129.4, 129.0, 128.7, 93.8, 79.4, 72.6, 61.8, 28.3, one carbon was not found probably due to overlapping; IR (neat): 3433, 3033, 2978, 1714, 1634, 1491, 1367, 1227, 1166, 1095, 754 cm^{-1}; HRMS (FAB) Calcd for $C_{28}H_{28}N_2O_4SCl^+$ ($[M+H]^+$) 523.1458. Found 523.1446.



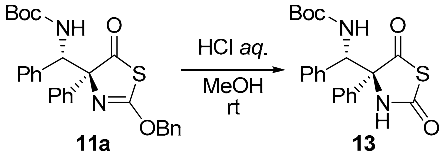
11j: HPLC: AD-H, H/IPA = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 10.1 min (minor *anti* isomer), 10.8 min (major *anti* isomer), 14.7 min (major *syn* isomer), 28.4 min (minor *syn* isomer), Absolute and relative configurations were assigned on the analogy of **11a**; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 7.52-7.32 (6H, m), 7.24-7.16 (7H, m), 7.14-7.08 (2H, m), 6.76 (1H, d, J = 10.0 Hz), 5.64 (1H, d, J = 12.0 Hz), 5.61 (1H, d, J = 12.0 Hz), 5.24 (1H, d, J = 10.0 Hz), 3.48 (1H, d, J = 13.0 Hz), 3.28 (1H, d, J = 13.0 Hz), 1.43 (9H, s); ^{13}C NMR (126 MHz, $(CD_3)_2CO$) for major *anti* isomer δ 208.3, 161.9, 156.2, 138.6, 136.7, 135.6, 131.5, 129.7, 129.5, 129.3, 128.7, 128.5, 127.6, 93.7, 79.7, 72.0, 60.9, 42.6, 28.6, two carbons were not found probably due to overlapping; IR (neat): 3426, 3032, 2979, 1715, 1633, 1495, 1367, 1218, 1166, 754 cm^{-1}; HRMS (FAB) Calcd for $C_{29}H_{31}N_2O_4S^+$ ($[M+H]^+$) 503.2005. Found 503.1992.

(5) Derivatization of 11a:

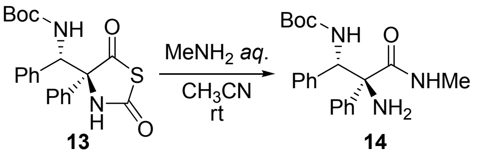


Procedure for derivatization of 11a to 12: A solution of **11a** (*anti*/*syn* = 10:1, 99% ee for *anti* isomer) (24.9 mg, 0.0533 mmol) in THF (5.3 mL) was treated with 30% H_2O_2 aqueous solution (315.0 μL) and a 1.0 M LiOH aqueous solution (530.0 μL, 0.53 mmol) at room temperature for 20 h. Then, a saturated aqueous solution of Na_2SO_3 was added until peroxides were completely reduced. The resulting mixture was acidified with 2 M $KHSO_4$ aqueous solution and extracted with EA twice. The organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure to give the crude carboxylic acid. In the presence of K_2CO_3 (29.3 mg, 0.212

mmol), MeI (7 μL, 0.106 mmol) was added to a solution of the obtaining acid in DMF (0.18 mL) at 0 °C, and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O and extracted with ether twice. After concentration of the organic extracts, purification of the residue by column chromatography on silica gel (H/EA = 10:1-3:1 as eluent) gave diastereomerically pure **12** as a white solid (17.8 mg, 0.0353 mmol, 66% in two steps) without loss of the enantiomeric purity. **12:** HPLC: AD-H, H/EtOH = 19:1, flow rate = 1.0 mL/min, λ = 210 nm, 6.9 min (major isomer), 8.1 min (minor isomer); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (1H, d, *J* = 8.5 Hz), 7.51 (2H, d, *J* = 7.5 Hz), 7.43-7.30 (8H, m), 7.25-7.20 (3H, m), 7.12 (2H, dd, *J* = 7.5, 2.0 Hz), 6.41 (1H, s), 6.22 (1H, d, *J* = 8.5 Hz), 5.22 (1H, d, *J* = 12.5 Hz), 5.07 (1H, d, *J* = 12.5 Hz), 3.71 (3H, s), 1.37 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 156.2, 156.1, 138.8, 136.3$_0$, 136.2$_8$, 128.7, 128.6, 128.5, 128.3, 127.9, 127.4, 127.3, 79.4, 70.6, 67.4, 59.0, 53.9, 28.6; IR (neat): 3395, 2978, 1713, 1504, 1455, 1366, 1269, 1168, 1053, 730 cm^{-1}; $[\alpha]_D^{28}$ -45.4° (c = 0.55, $CHCl_3$); HRMS (FAB) Calcd for $C_{29}H_{33}N_2O_6^+$ ([M+H]$^+$) 505.2339. Found 505.2331.



Preparation of 13 from 11a: Treatment of **11a** (*anti*/*syn* = 10:1, 99% ee for *anti* isomer) with 1 M HCl methanolic solution at room temperature for 30 min followed by purification by silica gel column chromatography (H/EA = 5:1-1:1 as eluent) furnished **13** as a white solid. **13:** ^{1}H NMR (500 MHz, CD_3OD) for major *anti* isomer δ 7.68 (2H, d, *J* = 7.5 Hz), 7.46 (2H, t, *J* = 7.5 Hz), 7.41 (1H, t, *J* = 7.5 Hz), 7.39-7.34 (3H, m), 7.32 (2H, d, *J* = 7.5 Hz), 6.93 (1H, d, *J* = 9.5 Hz), 5.82 (1H, br), 1.23 (9H, s) , a N-H proton was not found probably due to deuteration; ^{13}C NMR (126 MHz, CD_3OD) for major *anti* isomer δ 199.5, 167.2, 156.8, 137.7, 136.7, 130.2, 129.9, 129.8, 129.5, 127.4, 82.7, 81.0, 60.9, 28.4, one carbon was not found probably due to overlapping; IR (neat): 3292, 2979, 1710, 1685, 1523, 1395, 1245, 1161, 1065, 753 cm^{-1}; HRMS (FAB) Calcd for $C_{21}H_{23}N_2O_4S^+$ ([M+H]$^+$) 399.1379. Found 399.1383.



Conversion of 13 to 14: To a solution of **13** (*anti*/*syn* = 10:1) obtained as above in MeCN was added 40% aqueous solution of $MeNH_2$ at room temperature and the mixture was stirred for 30 min. After concentration to remove all volatiles, **14** was isolated by silica gel column chromatography ($CHCl_3$/MeOH = 1:0-5:1 as eluent) in 92% yield (two steps) without loss of the enantiomeric purity. **14:** HPLC: IA, H/EtOH = 19:1, flow rate = 1.0 mL/min, λ = 210 nm, 11.5 min (major *syn* isomer), 16.5 min (minor *syn* isomer), 21.5 min (major *anti* isomer), 25.4 min (minor *anti* isomer); ^{1}H NMR (500 MHz, CD_3OD) for major *anti* isomer δ 7.75 (2H, d, *J* = 7.5 Hz), 7.41 (2H, d, *J* = 7.5 Hz), 7.38-7.30 (4H, m), 7.27 (2H, t, *J* = 7.5 Hz), 6.13 (1H, s), 2.50 (3H, s), 1.27 (9H, s), N-H protons were not found probably due to deuteration; ^{13}C NMR (126 MHz, CD_3OD) for major *anti* isomer δ 176.0, 157.6, 142.2, 140.4, 129.5, 129.3, 129.0, 128.6, 128.3, 127.6, 80.2, 68.7, 59.6, 28.7, 26.3; IR (neat): 3363, 2978, 1693, 1653, 1520, 1496, 1411, 1365, 1248, 1168, 881, 754 cm^{-1}; HRMS (FAB) Calcd for $C_{21}H_{28}N_3O_3^+$ ($[M+H]^+$) 370.2131. Found 370.2115.

Crystallographic Structure Determination:

Recrystallization of 1a: Recrystallization of **1a** was achieved by using MeOH/toluene solvent system at −15 °C.

The single crystal thus obtained was mounted on CryoLoop. Data of X-ray diffraction were collected at 153 K on a Bruker SMART APEX CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). An absorption correction was made using SADABS. The structure was solved by direct methods and Fourier syntheses, and refined by full-matrix least squares on F^2 by using SHELXTL.[10] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in calculated positions and isotropic thermal parameters refined. The crystallographic data were summarized in the following table.

Table S1. Crystal data and structure refinement for **1a**·2MeOH·H_2O.

Empirical formula	C38 H41 N O4	
Formula weight	575.72	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 11.552(5) Å	α = 90°.
	b = 9.827(5) Å	β = 109.875(11)°.
	c = 14.569(7) Å	γ = 90°.
Volume	1555.4(13) $Å^3$	
Z	2	
Density (calculated)	1.229 Mg/m^3	
Absorption coefficient	0.079 mm^{-1}	
F(000)	616	
Crystal size	0.60 x 0.20 x 0.10 mm^3	
Theta range for data collection	1.49 to 28.39°.	
Index ranges	-15<=h<=15, -13<=k<=12, -14<=l<=19	
Reflections collected	11719	
Independent reflections	6478 [R_{int} = 0.0329]	
Completeness to theta = 28.39°	98.7 %	
Absorption correction	None	
Max. and min. transmission	0.9922 and 0.9543	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6478 / 1 / 399	
Goodness-of-fit on F^2	1.032	
Final R indices [I>2sigma(I)]	R1 = 0.0496, wR2 = 0.1157	
R indices (all data)	R1 = 0.0593, wR2 = 0.1216	
Largest diff. peak and hole	0.291 and -0.234 e.$Å^{-3}$	

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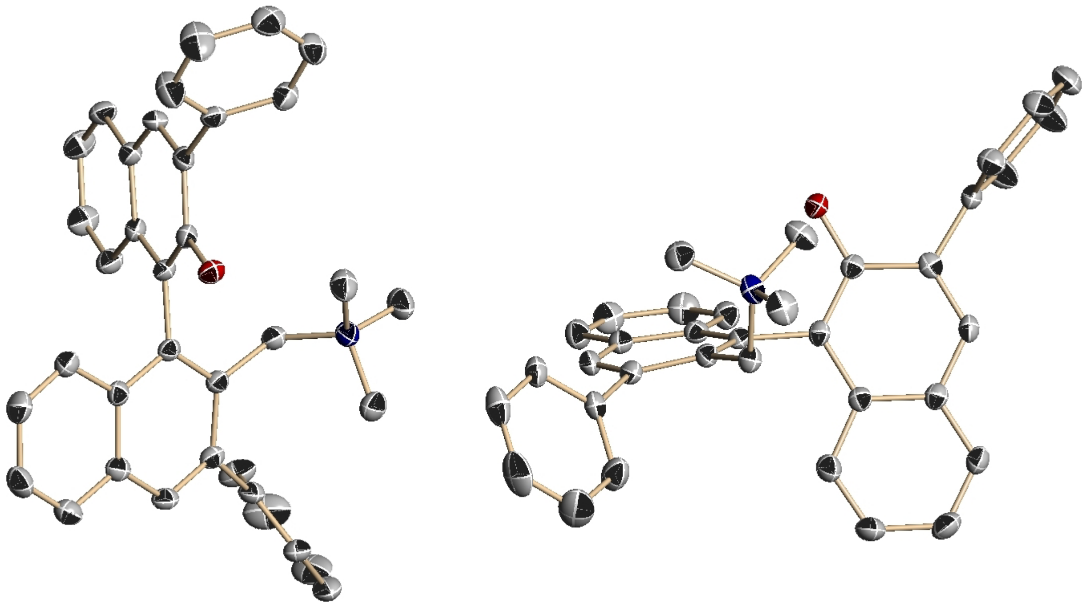
[10] Sheldrick, G. M. SHELXTL 5.1, Bruker AXS Inc., Madison, Wisconsin, 1997.



(a) Top view (b) Front view

Figure S1. Molecular structure of **1a**. All hydrogen atoms and solvent molecules are omitted for clarity. Blue = nitrogen, red = oxygen, black = carbon. The thermal ellipsoids of non-hydrogen atoms are shown at the 50% probability level.

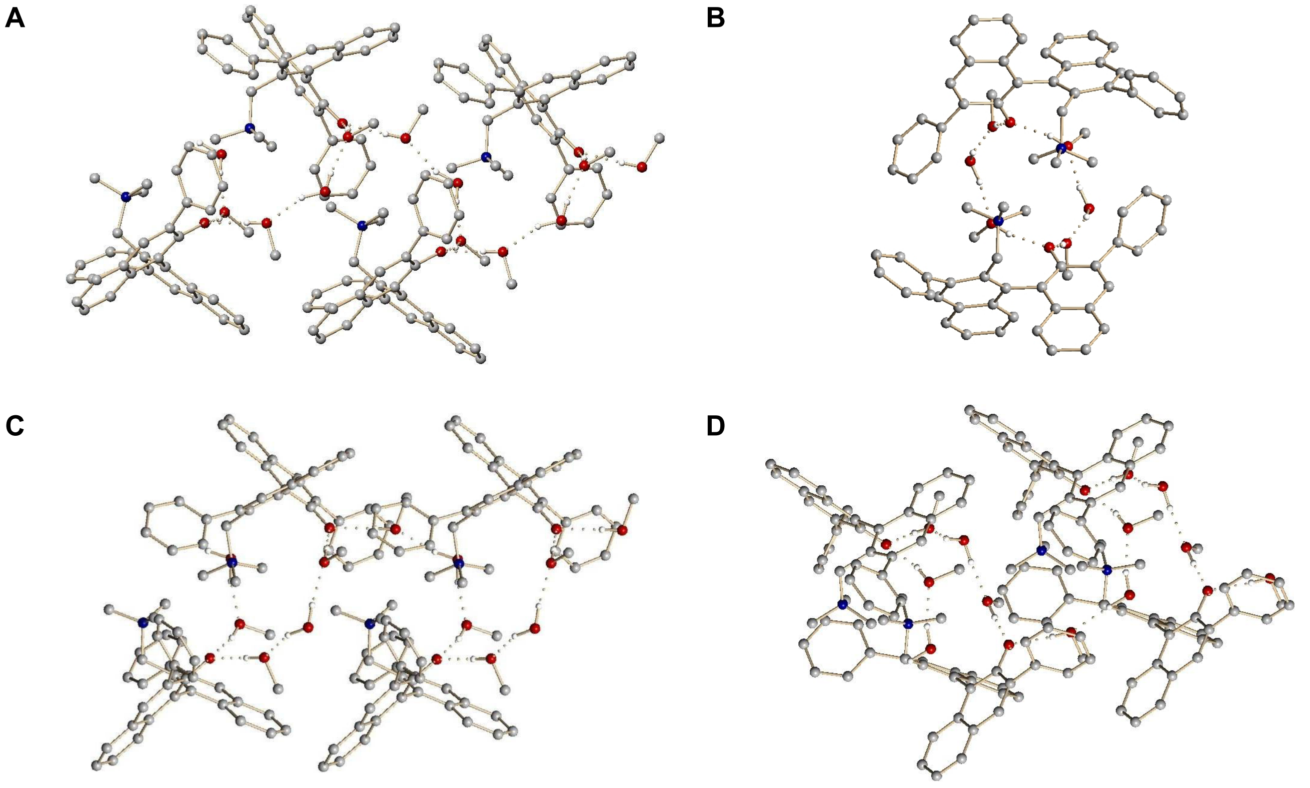


Figure S2. Packing model of **1a**. All hydrogen atoms except O-H protons are omitted for clarity. Blue = nitrogen, red = oxygen, black = carbon. The molecules form helical hydrogen-bonding network (···H-O-H···O(Me)-H···O$^-$(**1a**) ···H-O(Me) ···H-O-H···).

Recrystallization of *anti*-13: Recrystallization of *anti*-**13** was achieved by using CD_3OD as a solvent at room temperature.

The single crystal thus obtained was mounted on CryoLoop. Data of X-ray diffraction were collected at 153 K on a Bruker SMART APEX CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). An absorption correction was made using SADABS. The structure was solved by direct methods and Fourier syntheses, and refined by full-matrix least squares on F^2 by using SHELXTL.[10] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms bonded to nitrogen atoms were located from a difference synthesis and their coordinates and isotropic thermal parameters refined. The other hydrogen atoms were placed in calculated positions and isotropic thermal parameters refined. The crystallographic data were summarized in the following table.

Table S2. Crystal data and structure refinement for *anti*-**13**.

Empirical formula	C21 H22 N2 O4 S1	
Formula weight	398.47	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 11.7097(16) Å	α = 90°.
	b = 16.840(2) Å	β = 90°.
	c = 21.042(3) Å	γ = 90°.
Volume	4149.2(10) Å^3	
Z	8	
Density (calculated)	1.276 Mg/m^3	
Absorption coefficient	0.184 mm^{-1}	
F(000)	1680	
Crystal size	0.30 x 0.20 x 0.20 mm^3	
Theta range for data collection	1.55 to 28.33°.	
Index ranges	-15<=h<=15, -22<=k<=12, -28<=l<=27	
Reflections collected	31771	
Independent reflections	10322 [R_{int} = 0.0696]	
Completeness to theta = 28.33°	99.8 %	
Absorption correction	Empirical	
Max. and min. transmission	0.9641 and 0.9468	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10322 / 0 / 527	
Goodness-of-fit on F^2	1.084	
Final R indices [I>2sigma(I)]	R1 = 0.0627, wR2 = 0.1196	
R indices (all data)	R1 = 0.0824, wR2 = 0.1277	
Absolute structure parameter	0.01(7)	
Largest diff. peak and hole	0.430 and -0.224 e.Å^{-3}	

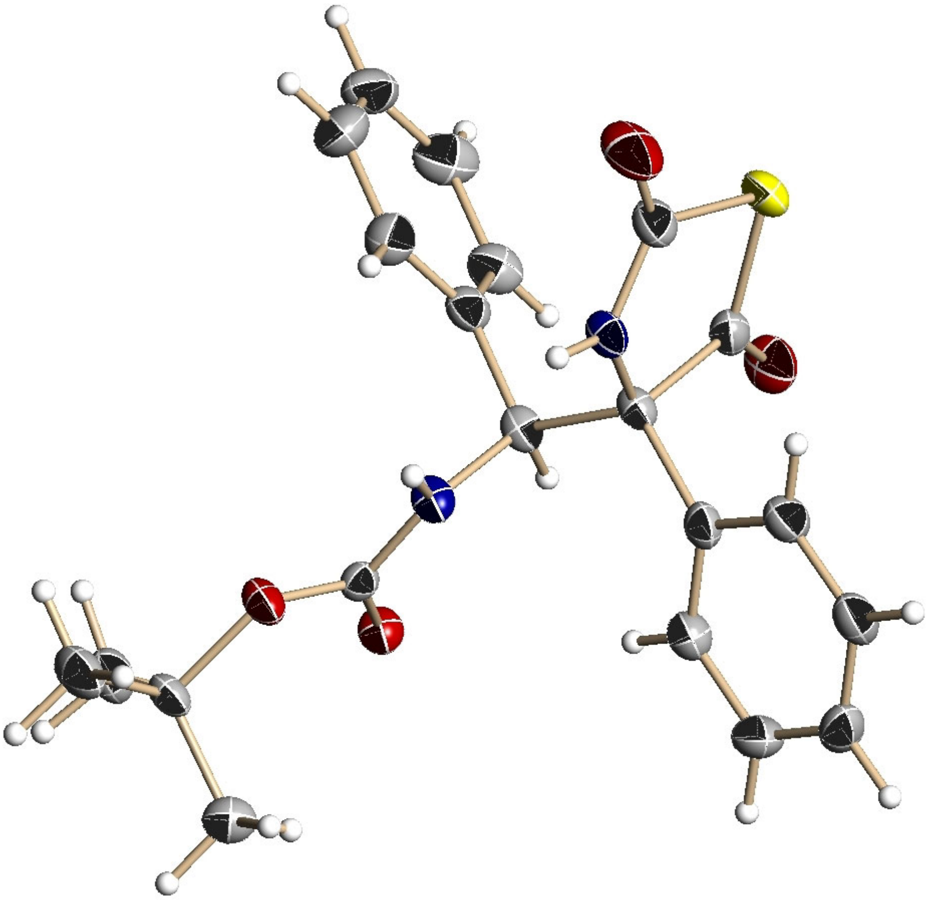


Figure S3. Molecular structure of *anti*-**13**. Blue = nitrogen, red = oxygen, yellow = sulfur, black = carbon. The thermal ellipsoids of non-hydrogen atoms are shown at the 50% probability level.